REMARKS

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments to the specification and claims and the following remarks.

Status of the Claims

In the present Amendment, claims 1, 5 and 10 have been amended, claim 15 has been added, and claims 12-14 have been canceled without prejudice or disclaimer of the subject matter contained therein. Also, claims 8-9 were previously canceled. Finally, claim 7 has been withdrawn from consideration. Thus, claims 1-7, 10, 11 and 15 are pending in the present application.

No new matter has been added with the present amendments and new claim. For example, the amendment to claim 1 actually deletes subject matter and is otherwise made for clarification purposes. The amendment to claim 5 is also clarifying in nature and is not narrowing in scope. Further, support for the amendment to claim 10 can be found in the Examples, such as page 22, lines 1-19 and page 35, line 23 to page 38, line 9 of the present specification (reference curves are also shown in some of the Figures). Finally, new claim 15 has support in the specification at page 16, lines 2-4.

No new matter has been added with the amendments to the present specification as typographical and grammatical errors are being corrected.

Based upon the above considerations, entry of the present amendment is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner

withdraw the objection and rejections and allow the currently pending claims.

Priority Document for Present Application

The Examiner has acknowledged Applicants' claim for priority for the present U.S. patent application. However, Applicants note that the copy of the Japanese Patent Application No. 2001-37115 filed at the time of filing this application (on February 14, 2002) is a certified copy. In this regard, Applicants herein enclose a copy of the first page of this priority document showing such certification. Thus, Applicants respectfully request acknowledgement and receipt from the Examiner regarding the certified copy of the Japanese Patent Application No. 2001-37115.

Claim Objection

Claim 12 stands objected to as stated on page 2, paragraph 3 of the Office Action. This objection is rendered moot due to the cancellation of claim 12 herein. Withdrawal of this objection is respectfully requested.

Issues Under 35 U.S.C. § 103(a)

Claims 1, 2, 3, 6 and 10 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan *et al.* (*J. Biol. Chem.*, Vol. 268, p. 20443-20451 (1993)) in view of Blain *et al.* (*J. Biol. Chem.*, Vol. 272, p. 25863-25872 (1997)), Jeong *et al.* (*BioTechniques*, Vol. 27, p. 1232-1238, (1997)), Facemyer *et al.* (*Bioconjug. Chem.*, Vol. 3, p. 408-413 (1992)) and Gray *et al.* '485 (newly cited; U.S. Patent No. 6,255,485) (see paragraph 4 of the outstanding Office Action).

Also, claims 4, 5, 13 and 14 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan *et al.*, Blain *et al.*, Jeong *et al.*, Facemyer *et al.*, and Gray '485 and in further view of Abo *et al.* '911 (U.S. Patent No. 5,518,911)) (see paragraph 5 of the Office Action).

Further, claims 11 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Pan *et al.*, Jeong *et al.*, Blain *et al.*, Facemyer *et al.*, and Gray '485 in further view of Gopalakrishna *et al.* (*Analytical Biochemistry*, Vol. 206, pp. 24-35 (1992)) (see paragraph 6 of the Office Action).

These rejections are respectfully traversed. Reconsideration and withdrawal thereof are respectfully requested.

The Rejection in view of Pan *et al.*, Blain *et al.*, Jeong *et al.*, Facemyer *et al.* and Gray '485

The Pan *et al.* reference is the primary reference cited for this 35 U.S.C. § 103(a) rejection.

Pan *et al.* describe a method of measuring activity of cdk2 or cdc2 which are isolated from HeLa cells. However, Pan *et al.* fail to disclose the several steps of the method as instantly recited in claim 1, including the following step:

> calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

The Examiner refers to several secondary references to account for the deficiencies of Pan *et al.* For instance, the Examiner next cites the Blain *et al.* reference. Blain *et al.* does

describe a method of measuring CDK activity found in the mink lung epithelial cell line (Mv1Lu). However, Blain *et al.* fail to disclose the several steps of the method as recited in pending claim 1, including:

> calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

Further secondary references are cited to account for the deficiencies of Pan *et al.* and Blain *et al.* For instance, the secondary reference of Jeong *et al.* is cited as describing a method of measuring protein kinase A (PKA) activity. In the Jeong *et al.* method, the fluorescein-labeled PKA substrate is "Kemptide" (see, e.g., the "*Materials and Methods*" section starting on page 1233). But in contrast, the present invention uses labeling of a substrate that is carried out after the enzyme reaction of CDK with the substrate. Therefore, Jeong *et al.* do not describe or suggest the present invention in this regard. Moreover, Jeong *et al.* fail to disclose the several steps of the present invention, including:

> calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

Facemyer *et al.* is also cited in forming the instant rejection. The cited secondary reference of Facemyer *et al.* describes a method of measuring activity of myosin light chain kinase that has been purified and isolated. Facemyer *et al.* describes that kinases which are known to use ATPγS as a substrate include phosphorylase kinase, cAMP dependent protein kinase, nuclear protein kinase II, cGMP dependent protein kinase, protein kinase C, kinase F_A,

heme-regulated protein kinase, calmodulin-dependent protein kinase II and EGF-receptor-associated protein kinase (see page 408, the "*Introduction*" section of Facemyer *et al.*). However, Facemyer *et al.* fail to disclose CDK. Moreover, Facemyer *et al.* fail to disclose the several steps of the method of the present claim 1, including:

> calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

Gray '485 is also cited in the instant rejection. The Gray '485 reference is directed to purine inhibitors of protein kinases, G proteins and polymerases (see the Abstract thereof). Further, Example 7 at columns 37-39 of Gray '485 describes measurement for CDK2 activity. In this disclosed measurement, a phosphate group is introduced from γ^{32}P-ATP to a substrate via CDK2, and the obtained substrate is blotted on a nitrocellulose membrane to measure the substrate (see, e.g., steps j and k in column 38). However, Gray '485 fails to disclose the several steps of the method of the present claim 1, including:

> calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

Accordingly, Applicants note that each and every one of the cited references is deficient in disclosing all claimed features. In particular, the cited combination of Pan *et al.*, Blain *et al.*, Jeong *et al.*, Facemyer *et al.* and Gray '485 still fails to disclose the following claimed step:

calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

U.S. case law squarely holds that a proper obviousness inquiry requires consideration of three factors: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they should make the claimed invention (or practice the invention in case of a claimed method or process); and (3) whether the prior art establishes that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Here, as mentioned, the cited combination of references still fails to disclose all instantly claimed features, including the mentioned calculation step.

Further, the requisite motivation is lacking. In this regard, it is not *prima facie* obvious to modify a reference unless the references suggest an advantage to be gained from the modification. *See In re Sernaker*, 217 USPQ 1, 6 (Fed. Cir. 1983). The cited references do not suggest any advantage to be gained by making the Examiner's proposed combination. Here, as just one instance, Pan *et al.*, Blain *et al.* and Jeong *et al.* fail to disclose catching CDK with an-CDK antibody and Facemyer *et al.* fail disclose anything regarding CDK as instantly claimed. Thus, under *Vaeck* and *Sernaker*, the requisite motivation is lacking and this rejection has been overcome. More specifically, the references do not suggest any advantage of catching CDK with an anti-cyclin-dependent kinase antibody, reacting ATP-γS, etc., as instantly claimed.

Thus, this rejection has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

Regarding independent pending claim 10, Applicants note that none of the cited combinations of references discloses or suggests the following claimed steps:

> adding a thiol to the buffer solution to stop the coupling between the sulfur atom and the labeling fluorophore or the labeling enzyme; and
>
> calculating the activity of the cyclin-dependent kinase from the measured amount of fluorescence or the measured amount of the generated product with reference to a pre-produced reference curve.

Therefore, instantly pending claim 10 is also patentably distinct from the cited combination of references. *In re Vaeck; supra.* Reconsideration and withdrawal of the rejection of claim 10 are respectfully requested.

The Rejection in view of Pan *et al.*, Blain *et al.*, Jeong *et al.*, Facemyer *et al.*, Gray '485 and Abo *et al.* '911

Applicants note that claims 4, 5, 13 and 14 are at issue here. First, claims 13-14 are canceled, which renders the rejection of these claims moot. Second, claims 4-5 ultimately depend on claim 1. Thus, the arguments presented above with respect to claim 1 also apply to claims 4-5 as well. Adding the citation of Ando '911 still does not cure the deficiencies of the initial combination of Pan *et al.*, Blain *et al.*, Jeong *et al.*, Facemyer *et al.* and Gray '485, or how these references are improperly combined, and thus a *prima facie* case of obviousness has not

been established. *In re Vaeck; supra.* Accordingly, reconsideration and withdrawal of the rejection of claims 4-5 are respectfully requested.

The Rejection in view of Pan *et al.*, Jeong *et al.*, Blain *et al.*, Facemyer *et al.*, Gray '485 and Gopalakrishna *et al.*

Applicants note that claims 11 and 12 are at issue here. First, claim 12 has been canceled which renders the rejection of this claim moot. Second, claim 11 depends on claim 1. Thus, the arguments presented above also apply to claim 11 as well. Adding the citation of Gopalakrishna *et al.* still does not cure the deficiencies of the initial combination of Pan *et al.*, Jeong *et al.*, Blain *et al.*, Facemyer *et al.* and Gray '485, or how these references are improperly combined, and thus a *prima facie* case of obviousness has not been established. *In re Vaeck; supra.* Accordingly, reconsideration and withdrawal of the rejection of claim 11 are respectfully requested.

Conclusion

A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact Eugene T. Perez (Reg. No. 48,501) at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: September 20, 2006

Respectfully submitted,

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First page of certified copy of Japanese Patent Application No. 2001-37115 (1 page)

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別紙添付の書類に記載されている事項は下記の出願書類に記載されている事項と同一であることを証明する。

This is to certify that the annexed is a true copy of the following application as filed with this Office

出 願 年 月 日
Date of Application: ２００１年 ２月１４日

出 願 番 号
Application Number: 特願２００１－０３７１１５

[ST.10/C]: [ＪＰ２００１－０３７１１５]

出 願 人
Applicant(s): シスメックス株式会社

２００２年 １月１８日

特 許 庁 長 官
Commissioner,
Japan Patent Office 及川耕造

出証番号 出証特２００２－３０００１６５